

RESPONSE

A. Status of the Claims

Claims 38-60 were pending at the time of the Restriction Requirement, with claims 51-52 and 55-60 withdrawn from consideration as being drawn to non-elected inventions. Claim 38 has been amended to recite an "isolated" hyperimmune serum-reactive antigen. Support for this amendment may be found at, for example, the third complete paragraph on page 27 of the specification. Claim 38 also has been amended to recite "antigenic fragments." Support for this amendment may be found at, for example, the first complete paragraph on page 28 of the specification. Claim 38 has also been amended to include the subject matter of claim 45 and to delete the subject matter directed to non-elected inventions. Claims 40-43, 46-47, 49, 53, and 55 have been amended to maintain proper antecedent basis in view of the amendments to claim 38. Claims 39 and 44-45 have been canceled. Thus, claims 38, 40-43, and 46-60 are pending, with claims 51-52 and 55-60 being withdrawn.

B. The Rejection Under 35 U.S.C. § 101 Is Overcome

Claims 38-48 were rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. The claims have been amended to recite an "isolated" hyperimmune serum-reactive antigen. Applicant, therefore, requests the withdrawal of this rejection.

C. The Claims Are Supported by Adequate Written Description

Claims 38-50, 53 and 54 are rejected under 35 U.S.C. § 112, first paragraph, for a lack of adequate written description. In particular, the Action does not consider the genus of "fragments" encompassed by the claims to be adequately described in the specification. Applicant traverses this rejection.

Current claim 38 is directed to a pharmaceutical composition comprising an isolated hyperimmune serum-reactive antigen comprising an amino acid sequence from any of SEQ ID

NOs: 32 or "antigenic" fragments thereof. As noted by the Examiner, written description for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics (*i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics), sufficient to show the Applicant was in possession of the claimed genus. The present specification provides adequate written description of the genus of antigenic fragments encompassed by the claims.

First, the specification provides the structure of SEQ ID NO: 32. In addition, the specification discloses that the method by which SEQ ID NO: 32 was identified involved using sera from individuals with antibodies against *S. epidermidis* (*see e.g.*, Specification, para. bridging p. 56-57; Example 3, and Table 1). By screening antigens against sera from such individuals, the method identifies those antigens with a proven capability to stimulate an immune response. Thus, the specification discloses both the structure and function of SEQ ID NO: 32.

With regard to "antigenic fragments" of SEQ ID NO: 32, the specification states that an antigenic fragment is defined as a fragment of the identified antigen, which is itself antigenic or may be made antigenic when provided as a hapten (Specification, p. 28, first complete para.). A representative number of antigenic fragments are disclosed in Table 1 of the specification. The fragments listed in the 5th column from the left in Table 1 are those that were experimentally confirmed to be antigenic (*see* Example 3). The fragments listed in the 3rd column from the left are those predicted to be antigenic by the program ANTIGENIC (*see* Specification, paragraph bridging pages 54-55). Additionally, the specification discloses that antigenic fragments would be expected to have structural attributes such as alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet forming regions, turn and turn-forming regions, coil and coil-forming

regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta-amphipathic regions, flexible regions, surface-forming regions, substrate binding regions, and high antigenic index regions of SEQ ID NO: 32 (*see* Specification, paragraph bridging pages 27-28).

In view of the above, the present specification provides sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics (*i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics), sufficient to show that Applicant was in possession of "antigenic fragments" of SEQ ID NO: 32. Applicant, therefore, requests the withdrawal of this rejection.

D. The Claims Are Enabled

Claims 38-50, 53 and 54 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Action acknowledges that the specification is enabling for an isolated hyperimmune serum reactive antigen comprising the amino acid sequence of SEQ ID NO: 32 and an antigenic fragment consisting of amino acids 6-28 of SEQ ID NO: 32, but argues that is not enabling for a fragment comprising amino acids 6-28 of SEQ ID NO: 32 or other fragments of SEQ ID NO: 32. Applicant traverses this rejection.

To be enabling within the meaning of 35 U.S.C. § 112, the application must contain a description sufficient to enable one skilled in the art to make and use the claimed invention without undue extensive experimentation. Moreover, the MPEP states that "[f]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner

without undue experimentation.” MPEP § 2164.02. The present specification satisfies these requirements.

As discussed in the preceding section, the specification provides the structure of SEQ ID NO: 32. This sequence was identified using sera from individuals with antibodies against *S. epidermidis* (see e.g., Specification, para. bridging p. 56-57; Example 3, and Table 1). In other words, this sequence was identified because of a demonstrated ability to stimulate an immune response in a subject. In addition, the specification discloses numerous confirmed and predicted antigenic fragments of SEQ ID NO: 32. In particular, the specification discloses the following fragments: amino acids 6-28, 54-59, 135-147, 193-205, 274-279, 284-291, 298-308, 342-347, 360-366, 380-386, 408-425, 437-446, 457-464, 467-477, 504-510, 517-530, 535-543, 547-553, 562-569, 573-579, 592-600, 602-613, 626-631, 638-668 and 396-449 of SEQ ID NO: 32 (see Table 1). The specification further discloses that antigenic fragments would be expected to have structural attributes such as alpha-helix and alpha-helix forming regions, beta-sheet and beta-sheet forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta-amphipathic regions, flexible regions, surface-forming regions, substrate binding regions, and high antigenic index regions of SEQ ID NO: 32 (see Specification, paragraph bridging pages 27-28). Thus, the Action’s allegations that the specification fails to disclose critical residues that are important for any function (see Action, p. 9) are misplaced.

With regard to making the claimed hyperimmune serum reactive antigens or antigenic fragments thereof, the specification teaches that hyperimmune serum reactive antigens or antigenic fragments thereof can be made by recombinant protein expression, in vitro translation, or peptide synthesis (Specification, paragraph bridging pages 13-14; first paragraph on page 32). The antigenicity of a particular sequence can be confirmed by seeing if it is bound by antibodies

in sera from individuals with antibodies against *S. epidermidis* as described in Example 3 of the specification. Based on these teachings, a person of ordinary skill in the art could make and use numerous antigenic fragments encompassed by the claims.

Applicant further notes that enablement does not require that every species of a generic class has to be shown in the working examples of the specification. Rather, representative examples in the specification are sufficient. MPEP § 2164.02; *see also In re Fisher*, 427 F.2d 833, 839 (CCPA 1970) (explaining that as long as the specification discloses at least one method of making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied). In addition, enablement is not precluded by the necessity for some experimentation such as routine screening. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988).

In view of the above, the present specification contains a description sufficient to enable one skilled in the art to make and use the claimed invention without unduly extensive experimentation. Applicant, therefore, requests the withdrawal of this rejection.

E. The Claims Are Definite

The Action rejects claim 39 under 35 U.S.C. § 112, second paragraph, as being indefinite for recitation of the phrase “of Table 1.” This rejection is moot in view of the cancellation of claim 39.

Claim 38 is objected to because it recites non-elected sequences. Claim 38 has been amended such that it only recites the elected SEQ ID NO: 32. Applicant, therefore, requests the withdrawal of the objection.

F. The Claims Are Novel Over Kimmerly

Claims 38-44, 45-49 and 53-54 are rejected under 35 U.S.C. § 102(b) as being anticipated by Kimmerly (AAG81977; WO200134809). The Action asserts that Kimmerly teaches a

hyperimmune serum-reactive antigen comprising a fragment of SEQ ID NO: 32 as evidenced by the alignment of AAG81977 with SEQ ID NO: 32 from position 321 to 676. Applicant traverses.

A claim cannot be anticipated by a reference if the allegedly anticipatory disclosure is not enabled. Mere naming or description of the subject matter is insufficient if it cannot be produced without undue experimentation. MPEP § 2121.01; *see also* *Elan Pharms, Inc. v. Mayo Found. for Med. Educ. & Research*, 304 F.3d 1221, 1228 (Fed. Cir. 2002) (stating “The anticipating reference ‘must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.’”). Kimmerly does not anticipate the current claims because Kimmerly does not provide an enabling disclosure of the claimed pharmaceutical composition.

Kimmerly discloses 4454 sequences, almost all with unknown function, allegedly from *S. epidermidis*. Kimmerly postulates that these sequences may be useful for eliciting an immunological response, but there does not appear to be any data demonstrating such an effect. The AAG81977 sequence appears to correspond to sequence 1047 in the Kimmerly reference. Kimmerly describes sequence 1047 as a “putative peptide of unknown function.” Furthermore, it appears that since sequence 1048 starts with a methionine encoded by a start codon, that Kimmerly only provided an EST analysis of the *S. epidermidis* genome but did not confirm that the sequence is actually translated into a protein. Kimmerly’s description of vaccines on pages 33 to 35 is very general and does not identify specific sequences for such purposes.

Kimmerly’s guess that one or more of the over 4,000 sequences listed in the Kimmerly specification may be useful in a pharmaceutical composition is not enabling as it would require undue experimentation to test all of these sequences in the absence of any guidance in the Kimmerly specification as to which sequences would likely be immunogenic and thus useful in a

pharmaceutical composition. Accordingly, the current claims are not anticipated by Kimmerly. Applicants, therefore, request the withdrawal of this rejection.

G. The Claims Are Novel Over Doucette-Stamm

Claims 38-44, 45-49 and 53-54 are rejected under 35 U.S.C. § 102(e) as being anticipated by Doucette-Stamm *et al.* (U.S. 6,380,370). The Action provides an alignment of SEQ ID NO: 32 of the presently claimed invention with SEQ ID NO: 4318 of the cited reference, which indicates that the sequences are 98.7% identical. Applicant traverses this rejection.

As noted above, a claim cannot be anticipated by a reference if the allegedly anticipatory disclosure is not enabled. Mere naming or description of the subject matter is insufficient if it cannot be produced without undue experimentation. MPEP § 2121.01; *see also* *Elan Pharms, Inc. v. Mayo Found. for Med. Educ. & Research*, 304 F.3d 1221, 1228 (Fed. Cir. 2002) (stating “The anticipating reference ‘must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject matter.’”). Doucette-Stamm does not anticipate the current claims because Doucette-Stamm does not provide an enabling disclosure of the claimed pharmaceutical composition.

Like the Kimmerly reference, Doucette-Stamm discloses thousands of sequences, almost all with unknown function, allegedly from *S. epidermidis*. Doucette-Stamm postulates that these sequences may be useful in pharmaceutical formulations, but there does not appear to be any data demonstrating this usefulness. In particular, Doucette-Stamm does not appear to provide any evidence that SEQ ID NO: 4318 is antigenic. Doucette-Stamm’s guess that one or more of the thousands of listed sequences may be useful in a pharmaceutical composition is not enabling as it would require undue experimentation to test all of these sequences in the absence of any guidance in the Doucette-Stamm specification as to which sequences would likely be immunogenic and thus useful in a pharmaceutical composition. Accordingly, the current claims

are not anticipated by Doucette-Stamm. Applicants, therefore, request the withdrawal of this rejection.

H. Conclusion

Applicants believe this paper to be a full and complete response to the Office Action dated October 2, 2007. Applicants respectfully request favorable consideration of this case in view of the above comments and amendments. Should the Examiner have any questions, comments, or suggestions relating to this case, the Examiner is invited to contact the undersigned Applicants' representative at (512) 536-5654.

Respectfully submitted,



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